

PERMANENT
ART 31 ABST**WHAT IS CLAIMED IS:**

1. An isolated corepressor polypeptide having an amino acid sequence which comprises at least one LXXLL nuclear receptor interacting NR box motif wherein L is leucine and X is any amino acid residue, said polypeptide operably interactable with a nuclear receptor to actively repress transcription of DNA.
2. The isolated polypeptide of claim 1, wherein said polypeptide is operably interactable with a nuclear receptor in one of a ligand-dependent and partially ligand-dependent manner.
3. The isolated polypeptide of claim 2, wherein the nuclear receptor comprises a class I or a class II nuclear receptor.
4. The isolated polypeptide of claim 3, wherein the nuclear receptor is selected from the group consisting of ER α , ER β , GR, PR, VDR, RAR α , RAR β , RAR γ and RXR α .
5. An isolated polypeptide encoded by the nucleotide sequence at set forth in Fig. 1D.
6. An isolated corepressor polypeptide essentially having an amino acid sequence as set forth at Fig. 1D comprising at least one modification of the amino acid sequence.
7. The isolated polypeptide of claim 6, wherein said modification comprises at least one point mutation in the region of the sequence from nucleotides 53 to 57.

8. The isolated polypeptide of claim 7, wherein the sequence from nucleotides 53 to 57 comprises the sequence LSKAA.
9. An isolated corepressor polypeptide having within its amino acid sequence at least two C-terminal binding protein interaction motifs, said first C-terminal binding protein interaction motif comprising the sequence PLDLTVR, and said second C-terminal binding protein interaction motif comprising the sequence VLDLSTK, said polypeptide operably interactable with a C-terminal binding protein (CtBP) corepressor in a pathway to repress expression of DNA.
10. The isolated polypeptide of claim 9, wherein the CtBP corepressor is selected from the group consisting of CtBP1 and CtBP2.
11. The isolated polypeptide of claim 9 comprising the amino acid sequence as set forth in Fig. 1D.
12. An isolated polynucleotide coding for the polypeptide of claim 1.
13. The isolated polynucleotide of claim 12 wherein the sequence of the polynucleotide comprises the polynucleotide sequence as set forth in Fig. 1D.
14. An isolated polynucleotide coding for the polypeptide of claim 6.
15. An isolated polynucleotide coding for the polypeptide of claim 9.
16. The isolated polynucleotide of claim 15, wherein the sequence of the polynucleotide comprises the polynucleotide as set forth in Fig. 1D.

17. An expression vector comprising the polynucleotide of any one of claims 12 -16 operably linked to a promoter for expression in a host cell.
18. A host cell stably transformed with the expression vector of claim 17.
19. An antibody that specifically binds to the polypeptide of claim 1.
20. An antibody that specifically binds to the polypeptide of claim 6.
21. An antibody that specifically binds to the polypeptide of claim 9.
22. A transgenic knock-out mouse comprising disruption in an endogenous gene which encodes for a corepressor polypeptide having a sequence as set forth in Fig. 1D, wherein said disruption has been introduced into its genome by a recombinant DNA construct stably integrated into the genome of said mouse or an ancestor thereof, wherein the disruption of the corepressor gene reduces expression of said corepressor causing altered active transcription of DNA associated with the corepressor.
23. The transgenic knock-out mouse of claim 22, wherein the altered active transcription of DNA is increased relative to wild type.
24. A method of modulating a cell comprising a gene which encodes for a corepressor polypeptide having a sequence as set forth in Fig. 1D, said method comprising the steps of introducing into said cell the isolated polynucleotide according to claim 6, whereby expression of the corepressor polypeptide is modulated.

25. A method of inhibiting ligand-dependent transactivation in a cell by one of a class I and class II nuclear receptor comprising subjecting said cell to a corepressor amount of the polypeptide of claim 1.
26. The method of claim 25, wherein the nuclear receptor is selected from the group consisting of $E\alpha$, $E\beta$, GR, PR, VDR, $RAR\alpha$, $RAR\beta$, and $RAR\gamma$.
27. A method of repressing nuclear-receptor mediated transcription in a cell comprising providing a ligand-dependent corepressor amount of the polypeptide of claim 1 to said cell.
28. A method of modulating steroid hormone signaling in a cell comprising providing a ligand-dependent corepressor amount of the polypeptide of claim 1 to said cell.
29. A method of regulating gene expression in a cell comprising providing the polypeptide as set forth at claim 9, wherein the polypeptide is operable to interact with at least one protein in a pathway to regulate gene expression.
30. The method of claim 29, wherein the protein comprises a C-terminal binding protein corepressor.
31. The method of claim 30 wherein the C-terminal binding protein corepressor is selected from the group consisting of CtBP-1 and CtBP-2.
32. Use of the corepressor polypeptide of claim 1 to inhibit ligand-dependent transactivation in a cell by one of a class I and class II nuclear receptor.

33. The use of claim 32, wherein the nuclear receptor is selected from the group consisting of ER α , ER β , VDR, RAR α , RAR β , and RAR γ .
34. Use of the corepressor polypeptide of claim 1 to repress nuclear-receptor mediated transcription in a cell.
35. Use of the polypeptide of claim 1 to modulate steroid hormone signaling in a cell.
36. Use of the polypeptide of claim 9 to regulate gene expression in a cell.
37. Use of the polypeptide of claim 1 in an assay to select, for therapeutic purposes, compounds that modulate transcription of gene expression associated with the polypeptide.
38. Use of the polypeptide of claim 9 in an assay to select, for therapeutic purposes, compounds that modulate transcription of gene expression associated with the polypeptide.
39. A method for assaying for compounds capable of modulating the activity of a corepressor polypeptide of claim 1 or an active variant thereof to actively modify transcription of DNA comprising the steps of:
- (a) providing a corepressor polypeptide of claim 1 or an active variant thereof;
 - (b) contacting the corepressor polypeptide with a nuclear receptor in the presence and absence of the compound; and
 - (c) measuring the modulation in activity of repression of DNA translation of the corepressor polypeptide.

40. A method for assaying for compounds capable of affording selective recruitment of the corepressor polypeptide of claim 1 in the presence of a ligand of a nuclear receptor, wherein the corepressor is operably interactable with the nuclear receptor to actively repress transcription of DNA in the presence of the ligand.

41. The method of claim 40, wherein the ligand comprises estrogen or an estrogen-like compound and the repressed DNA transcription products are implicated in hormone-dependent cancer.

42. The method of claim 41, wherein the hormone-dependent cancer is selected from the group consisting of hormone-dependent breast cancer and hormone-dependent uterine cancer.